Clinical Trial of Stem Cell Gene Therapy for Sickle Cell Disease

Grant Award Details

Clinical Trial of Stem Cell Gene Therapy for Sickle Cell Disease

Grant Type: Disease Team Therapy Development III

Grant Number: DR3-06945

Project Objective: Objective of the project is carry out a Phase 1 autologous gene modified stem cell transplant in Sickle cell patients. During the first year of the project, team produced cGMP lot of recombinant LV. Titer determination and other assays were performed and vector was released for clinical use. First patient was enrolled in the study. Leukapheresis product from the patient was used to produce the gene modified HSC (cell product). Product characterization were carried out. Product met all release criteria except for for transduction efficiency (VCN/cell 0.2 VC/cell (taget >0.3VC/cell). As a result patient was dosed. Team is the process of collecting second leukapheresis product which will be gene transduced and product number 1 and 2 will be combined to increase the cell dose.

Investigator:

Name:	Donald Kohn
Institution:	University of California, Los Angeles
Type:	PI

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Name:	Gary Schiller
Institution:	University of California, Los Angeles
Type:	Co-PI

Disease Focus: Blood Disorders, Pediatrics, Sickle Cell Disease

Human Stem Cell Use: Adult Stem Cell

Cell Line Generation: Adult Stem Cell

Award Value: $13,145,465

Status: Active

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Grant Application Details

Application Title: Clinical Trial of Stem Cell Gene Therapy for Sickle Cell Disease

Public Abstract: Sickle cell disease (SCD)results from an inherited mutation in the hemoglobin gene that causes red blood cells to "sickle" under conditions of low oxygen. It occurs with a frequency of 1/500 African-Americans, and is also common in Hispanic-Americans, who comprise up to 5% of SCD patients in California. The median survival based on 1991 national data was 42 years for males and 48 years for females. More recent data indicate that the median survival for Southern California patients with SCD is only 36 years, suggesting that serious problems exist regarding access to optimal medical care in this community. By twenty years of age, about 15% of children with SCD suffer major strokes and by 40 years of age, almost half of the patients have had central nervous system damage leading to significant cognitive dysfunction. These patients suffer recurrent damage to lungs and kidneys as well as severe chronic pain that impacts on quality of life. While current medical therapies for SCD can make an important difference in short-term effects, the progressive deterioration in organ function results in compromised quality of life and early deaths in ethnic populations who are generally adversely affected by health care disparity. Transplantation of bone marrow from a healthy donor as a source of new adult blood-forming ("hematopoietic") stem cells can benefit patients with SCD, by providing a source for life-long production of normal red blood cells. However, bone marrow transplant is limited by the availability of well-matched donors and the problems that arise from immune reactions between the cells of the donor and the patient. Thus, despite major improvements in clinical care of SCD patients, SCD continues to be a major cause of illness and early death.
The stem cell therapy approach to be developed by this Disease Team will be used to treat patients with SCD by transplanting them with their own bone marrow adult hematopoietic stem cells that are genetically corrected by adding a novel therapeutic hemoglobin gene that blocks sickling of the red blood cells. This approach has the potential to permanently cure this debilitating and common illness with significantly less toxicity than with a bone marrow transplant from another person. A clinical trial using stem cell gene therapy for patients with SCD will be performed by this multi-disciplinary Disease Team, combining world-leading experts in stem cell gene therapy, clinical bone marrow transplantation and the care of patients with sickle cell disease. Successful use of stem cell gene therapy for sickle cell disease has the potential to provide a more effective and safe treatment for this disease to a larger proportion of affected patients.

Statement of Benefit to California:	Development of methods for regenerative medicine using genetically-corrected human stem cells will result in novel, effective therapies that improve the health for millions of Californians and tens of millions of people world-wide. Sickle cell disease is an inherited disease of the red blood cells that results from a specific hemoglobin gene mutation. Sickle cell disease disproportionately afflicts poor minority patients in the State of California, causing severe morbidity, early mortality and high medical costs. We will perform a clinical trial to evaluate a novel treatment for patients with sickle cell disease, using their own adult blood-forming stem cells, after correcting the hemoglobin gene defect. Successful treatment of sickle cell disease using adult blood forming "hematopoietic" stem cells corrected with gene therapy may provide a clinically beneficial way to treat sickle cell disease with greater safety and wider availability than current options. The clinical trial to be performed will treat sickle cell disease patients from across the state of California through the network of institutions incorporated into this Disease Team. All scientific findings and biomedical materials produced from our studies will be publicly available to non-profit and academic organizations in California, and any intellectual property developed by this Project will be developed under the guidelines of CIRM to benefit the State of California.